PROGRESS / HEAL

SPECIAL ISSUE

FINDING A CONSENSUS

SPECIAL ISSUE AMERICAN LIVER FOUNDATION FALL 2002

Hepatitis C Consensus Conference Reviews New Treatments and Recommends All Patients Now Be Considered As Potential Candidates for Therapy

–Endows Hepatitis Clinical Research Network (HCRN)–

Substantial advances in the treatment for chronic hepatitis C were highlighted by a panel convened by the National Institutes of Health (NIH) during the first Management of Hepatitis C Consensus Conference to be held since 1997. The consensus panel broke away from its 1997 predecessors by expanding the range of patients eligible for treatment to include those who use injection drugs, consume alcohol, suffer from co-morbid conditions such as depression, or who are coinfected with HIV. Panelists also cautioned against the exclusion of children and older adults from treatment and further research. The conference was held in Bethesda, Maryland, June 10 through 12, and was attended by more than 1,200 scientists, physicians, patients and advocates.

Among its recommendations for future research, the panel gave top priority to the development of reliable and reproducible HCV cultures, which will advance the understanding of its biology, mechanisms of drug resistance, and aid vaccine development. ALF is pleased that the consensus panel also endorsed the ALF Hepatitis Council recommendation for the establishment of a Hepatitis Clinical Research Network (HCRN) to conduct research related to the natural history, prevention and treatment of hepatitis C. Studies to determine the efficacy of alternative medicines are needed. The panel also recommended the development of strategies to better prevent, diagnose, and treat the disease among injection drug users and the incarcerated population.

The clinical and socioeconomic challenges of hepatitis C are many. The challenge that lies ahead is made evident by the fact that, in this year alone, 8,000–to–12,000 people will lose their lives to hepatitis C. There are an estimated 4 million Americans who have been infected with hepatitis C, of whom 2.7 million are chronically infected, and, according to the Centers for Disease Control and Prevention (CDC), hepatitis C deaths will greatly increase by year 2010.

The 12-member consensus panel included representation from internal medicine, gastroenterology, hepatology, infectious diseases, pediatrics, family practice, oncology and a consumer. The panel members heard presentations from 28 hepatitis C experts, and reviewed an extensive body of medical literature, as well as reports based on systematic reviews of the medical literature prepared by the Johns Hopkins University School of Medicine Evidence-based Practice Center (EPC) under contract to the U.S. Agency for Healthcare Research and Quality (AHRQ). Established in 1977, NIH's Consensus Development Program is the premiere healthcare technology assessment and transfer program in American medicine. NIH Consensus Development Program conferences bring together biomedical research scientists, practicing physicians, and consumers in an effort to reach general agreement on whether a given medical technology – a device, a drug, or a medical or surgical procedure – is safe and effective.

"Combination therapies are having a beneficial impact on this disease," said panel chair James Boyer, M.D., Ensign Professor of Medicine and Director of the Liver Center at Yale University School of Medicine. "In addition, preliminary research indicates that this approach may prove useful in treating important subgroups of patients, including children and injection drug users, previously ineligible for treatment. Up to now, the majority of studies have focused on what is actually a narrow segment of the patient population. Thus, we still have a lot to learn."

The two and one-half day Conference focused on six overriding issues in HCV management:

- What is the natural history of hepatitis C?
- What is the most appropriate approach to diagnose and monitor patients?

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This special combined issue of **Progress** & **HEAL** addresses the recent consensus conferences in the United States and Switzerland covering the treatment advances for hepatitis B and C. We think you will find the information useful and that you will be amazed at the focused attention hepatitis B and C have received as a result.

The EASL International Consensus Conference on Hepatitis B was held in Geneva, Switzerland, September 13 and 14th. The objective of the conference was to provide an up to date overview on the current knowledge on chronic hepatitis B. Experts reviewed the latest scientific evidence on virology, epidemiology, natural history, therapy and prevention.

The National Institutes of Health Consensus Conference on the Management of Hepatitis C, held in Maryland from June 10 through the 12, featured global experts in the fields of epidemiology, virology, natural history, prevention and therapy of hepatitis C (HCV) banding together to present the latest HCV information. The highlights of the 31 presentations made to the Panel are outlined in detail in this issue, and provide an overview of some of the more compelling and controversial information that shaped the Consensus Statement prepared by the Consensus Development Panel.

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- What is the most effective therapy for hepatitis C?
- Which patients with hepatitis C should be treated?
- What recommendations can be made to patients to prevent transmission of hepatitis C?
- What are the most important areas for future research?

In total, 31 speakers, including ALF Hepatitis Council members Gary Davis, M.D., Karen L. Lindsay, M.D., Adrian M. Di Bisceglie, M.D., and Teresa L. Wright, M.D., presented the Panel with the most current data and information available regarding all aspects of hepatitis C. In addition, Alan P. Brownstein, President and CEO of the American Liver Foundation, addressed the panel from the podium as a representative of ALF's Hepatitis Council, where he called for a hepatitis C clinical trial group.

In addressing the Consensus Panel, Mr. Brownstein emphasized that there was a need "for a sense of urgency without creating a sense of panic," and that the best way to drive liver disease research would be with "a major investment in hepatitis C research with the creation of an NIH-funded Hepatitis Clinical Trial Group (HCTG) to support clinical research networks that accelerate the evaluation of new drugs that treat hepatitis C." The Consensus Development Conference embraced this recommendation by calling for the establishment of a Hepatitis Clinical Research Network (HCRN).

Following a day and a half of presentations and audience discussion, the Panel weighed the presented information in an all-night marathon, which resulted in a draft Consensus Statement completed sometime around 4:30 a.m. Panel Chair Dr. Boyer presented the Statement to Conference attendees a few hours later. The Conference room was filled to capacity as Dr. Boyer made his preliminary remarks and then read aloud the draft Statement. Chief among the many important findings and recommendations in the document were:

Prevalence

- There are 3.9 million Americans infected with hepatitis C, and of this group, 2.7 million are estimated to have chronic infection. However, these estimates are provided by the National Health and Nutrition Examination Survey (NHANES), a survey that largely excludes groups with a substantially increased prevalence of infection, such as persons who are incarcerated, homeless, or institutionalized due to mental illness. The prevalence of hepatitis C is presently believed to be at least 1.8 percent, making HCV the most common blood-borne infection in the United States. Persons aged 40 to 59 years have the highest prevalence of HCV infection, and in this age group, the prevalence is highest in African-Americans.

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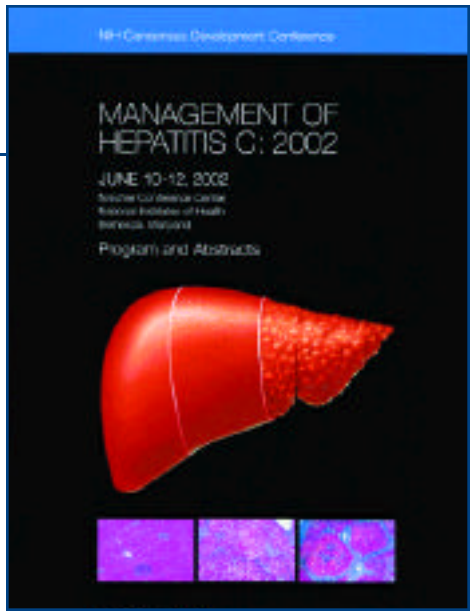
Conference Overview: New Information and Important Questions Emerge During Panel Presentations



Global experts in the fields of epidemiology, virology, natural history, prevention and therapy of hepatitis C presented the NIH Consensus Development Panel with the latest information. The highlights of the 31 presentations made to the Panel, outlined below, provide an overview of some of the more compelling and controversial information that shaped the Consensus Statement prepared by the Consensus Development Panel.

What is the Natural History of Hepatitis C?

During the Conference presentation, "The Course and Outcome of Hepatitis C," Jay H. Hoofnagle, M.D., explained that hepatitis C can cause both acute and chronic hepatitis.

Chronic hepatitis C is marked by persistence of HCV RNA for at least six months after the onset of infection. The chronicity rate of hepatitis C averages 70-80 percent, but varies by age, sex, race and immune status. Most patients with chronic hepatitis C have few if any symptoms, the most being fatigue, which is typically intermittent. Liver pain, nausea, and poor appetites occur in some patients. Serum ALT (alanine aminotransferase, a liver enzyme) levels are usually continuously or intermittently elevated, but the height of elevations correlates poorly with disease activity and at least one-third of infected persons have persistently normal ALT levels. For those patients, the underlying disease is usually, but not always, mild and non-progressive.

The major long-term complications of chronic hepatitis C are cirrhosis, end-stage liver disease, and liver cancer (hepatocellular carcinoma, HCC), which develop only in a portion of patients and only after many years or decades of infection. Progression to cirrhosis is often silent clinically and some patients are not known to have hepatitis C until they exhibit complications of end-stage liver disease or HCC. Once cirrhosis is present, the ultimate diagnosis is poor.

The course of hepatitis C is variable, the severity of illness ranging from a transient, self-limited and asymptomatic infection to a chronic, progressive liver disease that leads ultimately to cirrhosis and HCC.

What is the most appropriate approach to diagnose and monitor patients?

The Consensus Panel's Statement states that various tests are available for the diagnosis and monitoring of hepatitis C infection. Tests that detect antibody against the virus include the EIAs, which contain HCV antigens from the core and nonstructural genes, and the recombinant immunoblot assays (RIBAs). The same HCV antigens are used in both EIAs and the RIBAs. Targeted amplification techniques using either polymerase chain reaction (PCR) or transcription-mediated amplification (TMA) have been developed to detect HCV RNA. Liver biopsy can provide direct histologic assessment of liver injury due to HCV but cannot be used to diagnose HCV infection.

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A Message from the President and CEO

BY ALAN P. BROWNSTEIN

REACHING A CONSENSUS IS A TRIUMPH FOR THE LIVER DISEASE COMMUNITY

Over the past two years, ALF has diligently lobbied for a second NIH Consensus Development Conference on the Management of Hepatitis C. The recent conference represents an enormous success in the fight against hepatitis C. In preparation for the conference, ALF's Hepatitis Council created a position paper that was submitted to the Consensus Panel. I also had the honor of formally presenting an abbreviated version of ALF's statement at the meeting.

Our position paper called for a major investment in hepatitis C research with the creation of an NIH-funded Hepatitis Clinical Research Network (HCRN) to support clinical research networks that accelerate the evaluation of new drugs that treat hepatitis C, a recommendation endorsed by the Consensus Development Conference panel.

In addition to a clinical trials group, ALF articulated four principles to provide a foundation for the ongoing dialogues surrounding hepatitis C. They are:

- Hepatitis C awareness needs to be increased among those in the general public and in the medical community.
- Screening and diagnosis needs to be available to all who are at risk.
- Information about treatment options need to be shared with all who are diagnosed with hepatitis C, so that these patients are empowered with the information that they need to know to make decisions about their own lives and their own health in consultation with their physicians.
- Hepatitis C treatment must be available to all those who need it, regardless of their ability to pay.

The Consensus Panel fully recognized the importance of ALF's recommendations, and emphasized in its statement the importance of increased awareness by identifying the goal "to educate the American public on the transmission of HCV in order to better identify afflicted individuals and institute preventive measures."

With the support of our nationwide network of chapters and medical leaders, ALF will aggressively advocate the implementation of the recommendations contained in the Consensus report. ALF will also directly seek ways to educate the public and health care professionals about hepatitis C risks that may involve their patients as well as diagnosis and treatment recommendations.

I am grateful for the support we received from our medical, scientific and lay leadership in nationally driving the focus on hepatitis C. I am also proud of our government relations effort through which we secured Congressional support for the recent Consensus Conference. ALF is prepared to ensure that the initiatives developed in the Consensus Conference are fully realized.

Lastly, I wish to thank Dr. Jay Hoofnagle and his team at NIDDK for their leadership in supporting this conference as well as the efforts they will be expending in implementing the Consensus Conference recommendations.

We will continue to post Conference updates on the ALF Web site (www.liverfoundation.org) and will maintain a hot link to the NIH Web site.

NIH Consensus Panel Members

ALF extends its appreciation to all NIH Consensus Panel members (listed below) for their dedication and commitment to the important proceedings surrounding the conference.

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FOR MORE INFORMATION

For additional information about the NIH Consensus Development Conference on the Management of Hepatitis C, or to make inquiries concerning these proceedings, contact:

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EASL International Consensus Conference on Hepatitis B Held in Geneva, Switzerland

THE EUROPEAN ASSOCIATION FOR THE Study of the Liver (EASL) sponsored an International Consensus Conference on Hepatitis B in Geneva, Switzerland, on September 12-14.

The objective of the conference was to provide an update on the current knowledge of HbeAg positive and HbeAg negative chronic hepatitis B. Experts reviewed the latest scientific evidence on virology, epidemiology, natural history, therapy and prevention. Following the presentations, an independent jury panel produced a statement.

The independent jury panel addressed the following questions on the management of patients with chronic hepatitis B:

- What are the public health implications of hepatitis B?
- What is the natural history of hepatitis B virus infection, what are the factors influencing the disease?
- What is the best way to diagnose and classify hepatitis B?
- How can the transmission of hepatitis B be prevented?
- Which patients should be treated?
- What is the best treatment?
- How should untreated and treated patients be monitored?
- What are the main unresolved issues?

Juan Rodes (Spain) served as jury president; speakers included Miriam Alter and Theresa Wright (USA), Jenny Heathcote (Canada), Yun Fan Liaw (Taiwan), and Fabien Zoulim (France), among others.

Highlights of the meeting included complete review of the phase III trials of interferon, lamivudine and adefovir in the treatment of patients with chronic hepatitis B disease, including those who are HBeAg positive and negative; review of preliminary information about the use of pegylated interferon for chronic hepatitis B; and review of planned studies for pegylated interferon in combination with lamivudine.

The conference also highlighted our success in the management of hepatitis B disease in patients undergoing liver transplantation. In a decade, with effective interventions, we have markedly reduced the risk of post-transplantation recurrence, while at the same time expanding the donor pool through the use of anti-B core positive donors in select individuals.

A full summary of the Hepatitis B Consensus Conference recommendations are forthcoming and will be featured in the next issue of Progress and HEAL.

Spotlight: James Boyer, M.D.

Progress/Heal is very happy to have caught up with James Boyer, M.D., who served as Panel and Conference Chairperson. Dr. Boyer serves as Ensign Professor of Medicine, the Departments of Internal Medicine and Digestive Diseases, and Director of the Liver Center, Yale University School of Medicine.

Question: Dr. Boyer, What is the point of another Consensus Conference on the Management of Hepatitis C? Weren't all of our questions answered during the 1997 Conference?

Boyer: There have been great developments since the 1997 hepatitis C Consensus Conference. The recent conference was meant to be an update to the original consensus conference, so we didn't have to reinvent the wheel.

Question: How were the Conference panelists selected?

Boyer: Planning for the conference began in 2001, almost a whole year ahead. The planning committee widely represented the community and many of the NIH programs. Selecting panelists is a complicated process. It's an independent panel; members have to be non-advocate and non-federal/NIH. An extensive vetting process is held to make sure there are no conflicts of interest. Panelists can't have any financial relationship with any of the companies that sponsor the drugs used in hepatitis C treatment. They have to be experts in the area of science but they cannot be involved in any supported activities. For that reason, there were very few liver specialists on the panel. Many of the panel members were infectious disease experts, HIV experts or drug trial experts. There were two gastroenterologists and two hepatologists of the panel of 12 and none of those four had direct involvement with treatment programs for hepatitis C.

Question: What do you see as the significant changes made in the world of hepatitis C since 1997?

Boyer: One of the most significant changes since the last Consensus Conference is the better success of combination therapy. Combination therapy was just beginning to be studied at the time of the last conference, so we couldn't make any recommendations about its effectiveness. Since then, there are better standards of care with not only the combination of interferon and ribavirin, but with the combination of pegylated interferon and ribavirin. The ability to treat once a week (as with pegylated interferon) rather than three times a week (as with regular interferon) is significant for most types of chronic hepatitis C. Sustained viral response (SVR, or clearance of the virus

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Panel Recommendations Address ALF Issues

Prior to the convening of the NIH Consensus Conference, the American Liver Foundation's Hepatitis Council made several recommendations to the Consensus Development Panel charged with drafting the HCV Consensus Statement. Several of ALF's recommendations were reflected in the outcome of the proceedings and the Statement of the Consensus Panel.

ALF Hepatitis Council Recommendations	Consensus Conference Final Statement
Hepatitis C awareness must be increased among the general public and within the medical community. The primary targets of this campaign should include vulnerable population groups, including African Americans, Hispanics and Vietnam veterans, and those individuals who may be at risk through blood transfusions received before 1992, injection drug use, HIV coinfection or blood-to-blood contact. Primary care physicians must be equipped with information to optimize recognition and effective management of hepatitis C, with appropriate support from specialists.	• The panel's first recommendation was to educate the American public on the transmission of HCV in order to better identify affected individuals and to institute preventive measures. • Institute measures to reduce transmission of HCV among injection drug users (IDUs), including providing access to sterile syringes through needle exchange, physician prescription, and pharmacy sales; and expanding the Nation's capacity to provide treatment for substance abuse. Physicians and pharmacists should be educated to recognize that providing IDUs with access to sterile syringes and education in safe injection practices may be life-saving.
Screening and diagnosis should be available to everyone who needs it. Any American who may be at risk of hepatitis C infection, or who exhibits symptoms of the disease or is concerned over possible infection, should undergo a hepatitis C antibody test. Individuals who test positive should be further tested and referred for medical management. All avenues for access to care should be readily available to a patient and physicians once a treatment course has been decided. Reimbursement and/or coverage obstacles, as are evidenced by the thousands of calls that come to the ALF HelpLine, compromise too many hepatitis C patients. Future issues that the hepatitis community must address include patient access to health care coverage, the special needs of Vietnam veterans and the uninsured. For the medically indigent, this demands the exploration and development of appropriate government assistance mechanisms.	The first recommendation in patient treatment reads: "all patients with chronic hepatitis C are potential candidates for antiviral therapy." • Promote the standardization and wide availability of diagnostic tests for HCV infection and its complications, leading to early diagnosis and the implementation of appropriate treatment practices. • Promote the establishment of screening tests for all groups at high risk of HCV infection, including IDUs and incarcerated individuals.
Information regarding treatment options should be available to anyone who needs it. All patients diagnosed with hepatitis C, regardless of hepatitis profile, should be provided with the full spectrum of available information. This includes treatment options, risks and benefits of specific treatments, and the probablility of therapeutic success associated with them. This is the essential foundation of an educated and informed patient base. Treatment is, ideally, a decision made jointly by a patient in consultation with his or her physician.	This was not addresses by the Consensus Panel. It therefore becomes the responsibilty of the American Liver Foundation, and other liver health advocacy groups, to ensure that information about treatment options and emerging therapies are available to the public. The American Liver Foundation has two toll-free numbers where callers can get information on hepatitis C; they are **800.GO.LIVER** and **888.4HEP.USA**. In addition, news on emerging therapies is available at the American Liver Foundation Web site, **www.liverfoundation.org**.

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ALF's Impact on Conference *continued from page 5*

Effective hepatitis C treatment must be available to anyone who needs it.

All avenues for access to care should be readily available to a patient and physician once a treatment course has been decided. As with testing, reimbursement and/or coverage obstacles compromise too many hepatitis C patients. It is critically important that the Consensus Development panel clearly emphasize in its report that all patients should have equal access to treatment regardless of the source of health care coverage. For the medically indigent, this demands the exploration and development of appropriate government assistance mechanisms.

"Many patients with chronic hepatitis C have been ineligible for trials because of injection drug use, significant alcohol use, age, and a number of co-morbid medical and neuropsychiatric conditions. Efforts should be made to increase the availability of the best current treatments to these patients. Because a large number of HCV-infected persons in the United States are incarcerated, programs should be implemented to prevent, diagnose, and treat HCV infection in these individuals."

- Although it is likely that HCV is highly prevalent in patient populations without health insurance or with publicly funded health care payers, no data to support this are available. The prevalence of HCV infection and the feasibility of management and treatment in these populations should be studied.

The ALF calls for a major investment in hepatitis C of a sort never seen before, by the federal government and the private sector, in the form of an NIH-funded Hepatitis Clinical Trial Group (HCTG) to first identify, and then coordinate and provide funding for, existing networks and the establishment of new networks to conduct research into treatment of hepatitis C.

- Given the large number of persons with chronic HCV, the large number of untreated patients, and a compelling number of important areas for future research, we recommend that the NIH establish a **Hepatitis Clinical Research Network**. The goal of this network should be the conduct of research related to the natural history, prevention, and treatment of hepatitis C.

Hep C Conference *continued from page 2*

Diagnosis

- There are many different ways of assessing the presence of hepatitis C virus infection. Tests that detect antibodies against the virus include the EIAs, which contain HCV antigens from the core and nonstructural genes, and the recombinant immunoblot assays (RIBAs). The same HCV antigens are used in both EIAs and the RIBAs. A liver biopsy also plays an important role – although it cannot be used to diagnose HCV infection, a liver biopsy is used to define the amount of liver damage as a result of hepatitis C.

Treatment

- Several important therapeutic advances have occurred since the 1997 NIH Consensus Conference, including the introduction of pegylated interferon with ribavirin therapy. Combination therapy results in better treatment responses than monotherapy. The highest response rates have been achieved with pegylated interferon in combination with ribavirin. The type of virus a patient has (i.e. the HCV genotype) helps determine treatment decisions, including the duration of treatment and the dose of ribavirin to be used.

- Patients who may benefit from re-treatment include those whose HCV infection failed to achieve a sustained viral response (SVR). Decisions regarding re-treatment should be based upon: (1) previous type of response, (2) the previous therapy and the difference in potency of the new therapy, (3) the severity of the underlying liver disease, (4) viral genotype and other predictive factors for response, and (5) tolerance of previous therapy and adherence.

Future Areas of Research

- To achieve the above, molecular research efforts are needed on several fronts to improve the understanding and care of hepatitis C. The development of reliable, reproducible and efficient culture systems for propagating the HCV virus is considered to be of the highest priority.

- The Panel also recognized ALF's call to establish a Hepatitis Clinical Research Network for the purpose of conducting research related to the natural history, prevention and treatment of hepatitis C.

Following the formal reading to the draft Statement, an overwhelming number of audience members rose to request amendments, deletions or corrections to the document. Subsequent to the Conference, ALF wrote to the panel voicing concern over the removal of the specific reference to Vietnam veterans being at high risk, based on two or three requests made from the floor. "We believe this is an unfortunate error because it trivializes the fact that the rates among veterans, for whatever reasons, are high – at least three times that of the general population," the letter read.

ALF's follow-up letter also made specific mention of liver transplants and emerging techniques: "Studies are also needed to help close the gap between supply and demand for livers, including developing artificial organs, hepatocyte transplantation, xenotransplantation, live donor liver transplantation, split liver transplantation, and other research focuses as appropriate."

The Consensus Panel distributed a revised draft of the Statement, reflecting many of the comments made during the audience discussion, to the media during a press conference later that afternoon.

ALF presented its formal document of recommendations to the Panel at the beginning of the Conference (see "ALF's Impact," page 5). In the weeks following the Consensus Conference, ALF submitted its formal suggestions and feedback to the Panel for further consideration. The final draft of the Consensus Statement appeared in September 2002 and is available on the ALF Web site, www.liverfoundation.org.

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What is the most effective therapy for hepatitis C?

Adrian M. Di Bisceglie, M.D., believes that there has been considerable progress made in therapy since the last Consensus Development Conference on the Management of Hepatitis C in 1997. Using the sustained virologic response (SVR) rate as the standard definition of beneficial outcome of therapy, different treatments can be compared in various categories of patients. The combination of interferon alfa-2b and ribavirin resulted in SVR rates of 31-35 percent after a 24-week course and 38-43 percent after a 48-week course of therapy. The use of pegylated rather than standard interferon with ribavirin increased the response rate to 54-56 percent.

Dr. Mitchell L. Schiffman answered questions about retreatment of patients with chronic hepatitis C. Dr. Shiffman observes that a large number of patients who have been treated with alpha interferon with or without ribavirin did not achieve a sustained virologic response (SVR). As new therapies are developed for hepatitis C, the issue of retreatment of these non-responders will continue to arise.

Recommendations regarding retreatment should be based upon several factors: (1) the previous type of response, (2) the previous therapy and the difference in potency of the new therapy, (3) the severity of the underlying liver disease, (4) viral genotype and other predictive factors for response, and finally (5) tolerance of previous therapy and compliance.

Dr. Shiffman also reminds readers that an important reason for relapse and non-response to interferon therapy of hepatitis C is non-compliance. Non-compliance can be the result of severe side effects and inadequate management. If the causes of non-compliance can be corrected or lessened, retreatment can be successful. In contrast, if side effects are intolerable despite adequate counseling and management, retreatment is unlikely to be successful and should not be encouraged.

Which patients with hepatitis C should be treated?

Bruce R. Bacon, M.D., reminded Panelists that the 1997 Consensus Conference ended with the recommendation that "… treatment of patients with persistently normal ALT is not beneficial and may actually induce liver enzyme abnormalities."

However, since that time, according to Dr. Bacon, this issue has been controversial, with some investigators supportive of treatment and others suggesting that no work-up or therapy is necessary for these patients. Approximately 30 percent of patients with chronic hepatitis C have normal ALT levels, and another 40 percent have ALT levels that are less than two times the upper limit of normal. Most patients with normal ALT levels have mild degrees of inflammation with mild or no fibrosis and their rate of disease progression is reduced compared to those with elevated ALT levels. However, some patients with persistently normal ALT levels can progress to advanced fibrosis and cirrhosis.

The issue regarding treatment of these patients has often focused on how to proceed in patients with mild disease, recognizing that ALT levels may actually be just a proxy for mild histology. The best treatment trials that have been performed are the registration trials for FDA approval, and those have all required

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James Boyer *continued from page 4*

after completion of either six months or a year of treatment followed by six months of no treatment) with combination therapy is better than with monotherapy.

Question: What do the Conference findings mean for the average person with hepatitis C?

Boyer: Some of the consensus statement is highly scientific and would not be of much relevance to the average person. But, the average person will be able to see what the general recommendations are for treatment of the disease. The field of patients eligible for treatment has greatly expanded. Children, the elderly, patients with acute hepatitis C, injection drugs users or people in drug treatment programs were all formerly excluded from recommendations for treatment in 1997 and they have now been brought in.

Question: What do the Conference findings mean for the medical and scientific community?

Boyer: For the medical and scientific community, the consensus draft document provides clear guidelines for the management of hepatitis C. There are still some controversial areas, of course. In the revised draft, there is a little bit more clarification of the treatment management guidelines in terms of 'do treat' or 'do not treat.'

Question: How useful do you find the Consensus Conference format?

Boyer: The panel was able to assimilate a tremendous amount of complicated information under considerable time constraints. Many contributions from the presenters and from the floor were extremely useful and, in the majority of cases, were incorporated into the consensus report. The panel really did an admirable job. The format of the consensus conference, however, is perhaps a little bit too confining. There was not enough time for all the presenters to impart all the information they wanted to and not enough time for the consensus conference to really deal with many issues. There are more areas in this field that need to have emphasis put on them. I think that would be my only observation about the process.

Question: How effective do you see the consensus conference in driving forward the discussion surrounding hepatitis C?

Boyer: One of the most important things that we should glean from the Consensus Conference - particularly those of us who are able to help support research - is that the number of patients with chronic hepatitis and complications is going to grow over the next 10-15 years. Fortunately, the number of new infections is decreasing. Because this disease tends to become chronic in the majority of patients, we're now seeing a rise in the number of chronic cases. There's much more to do in terms of medical research and continued work in the areas of drug development, for which research and research dollars are going to be very badly needed.

Question: What are your thoughts (if any) on the panel's recommendations?

Boyer: If this consensus conference proves to be as effective as the first one -- and I see no reason why it shouldn't be even more so -- it will provide a major focus for future guidelines for treatment and for research.

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that patients have elevated ALT levels to be included in the study. There are no large treatment trials of normal ALT patients, although a few studies of interferon plus ribavirin in chronic hepatitis C patients with normal or near normal ALT levels have been reported.

There are numerous factors that impact on the decision to treat patients with mild liver disease, including genotype, histology, patient motivation, symptoms, comorbid illness, and the age of the patient. ALT levels may have less importance in deciding who should be treated. It no longer seems reasonable to conclude that SVR rates for patients with normal ALT levels are any different than those for patients with elevated ALT levels.

What are the most important areas for future research?

John G. McHutchinson, M.D., believes that, although current therapies are effective in more than half of all treated patients, therapy is costly, associated with significant morbidity, requires substantial commitment from the patient and medical staff, and is not suitable for all patients. Therefore, there is an important need for more effective therapies, and this remains a priority in terms of continued research endeavors. The ideal therapy for patients with chronic hepatitis C would be cost-effective, be orally bioavailable, have an acceptable side effect profile, and be effective in the majority of patients. Such therapies are probably unlikely to be developed in the near future.

However, the Consensus Panel's Statement calls for several important research initiatives. The development of reliable, reproducible, and efficient culture systems for propagating the HCV virus is considered to be of the highest priority. Also, priority should be given to developing less toxic therapies and molecular-based agents that specifically inhibit viral replication and/or translation of viral RNA.

Perhaps the most important step in the future research of hepatitis C is the recommendation of the establishment of a Hepatitis Clinical Research Network. The goal of this network, proposed from the podium by ALF President and CEO Alan P. Brownstein, is to conduct research related to the natural history, prevention, and treatment of hepatitis C.

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Web site: www.liverfoundation.org
E-mail: info@liverfoundation.org
The American Liver Foundation is a national voluntary health organization dedicated to the prevention, treatment, and cure of hepatitis and other liver diseases through research, education and advocacy.

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